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ORIGINAL ARTICLE

Improved respiratory parameters with skin-to-skin contact in premature infants with bronchopulmonary dysplasia on NIV-NAVA

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Abstract

Aim: To determine if skin-to-skin contact (SSC) improved respiratory parameters in premature infants with evolving or established bronchopulmonary dysplasia (BPD) on non-invasive neutrally adjusted ventilator assist (NIV-NAVA).

Methods: Premature infants (<32 weeks gestational age) with BPD on NIV-NAVA were studied. Continuous readings from the Edi catheter (modified nasogastric feeding tube inserted for NAVA ventilation) were compared: *pre-SSC* (baby in incubator) and *end-SSC* (just before end of SSC).

Results: Sixty-five episodes of SSC were recorded in 12 premature infants with median gestational age at birth of 24.4 (23.1–27.0) weeks and birth weight of 642 (530–960) grams. Peak Edi (uV) in *end-SSC* 11.5 (2.7–38.7) was significantly lower compared to *pre-SSC* 15.8 (4.0–36.6), $p < 0.001$. P mean (cmH_2O) was significantly lower in *end-SSC* 9.7 (7.3–15.4) compared to *pre-SSC* 10.3 (7.5–15.5), $p = 0.008$. Respiratory rate (breaths/min) was significantly lower in *end-SSC* 52.9 (31.1–78.1) compared to *pre-SSC* 53.4 (35.1–74.1), $p = 0.031$. There was no significant difference in inspired oxygen requirement or time on back-up mode in *end-SSC* 40.0 (22.1–56.1) and 5.9 (0.0–56.0) compared to *pre-SSC* 39.0 (26.0–56.1) and 5.1 (0.0–29.3), $p = 0.556$ and $p = 0.853$ respectively.

Conclusion: SSC improved respiratory parameters in premature infants with evolving or established BPD on NIV-NAVA.

KEYWORDS
neonatal trigger ventilation, neurally adjusted ventilatory assist, non-invasive ventilation, prematurity, skin-to-skin contact

Abbreviations: BPD, bronchopulmonary dysplasia; BW, birth weight; CGA, corrected gestational age; ECG, electrocardiogram; Edi, electrical activity of the diaphragm; FiO2, fraction of inspired oxygen; GA, gestational age; NAVA, neurally adjusted ventilatory assist; NIV, non-invasive ventilation; NIV-NAVA, non-invasive neutrally adjusted ventilator assist; P mean, mean airway pressure; Peak Edi or Edi peak, peak electrical activity of the diaphragm; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; RR, respiratory rate; SSC, skin-to-skin contact; WHO, World Health Organization.

1 | INTRODUCTION

The World Health Organization (WHO) endorses skin-to-skin (SSC) for the routine care of newborns weighing 2000 g or less at birth and recommends that this should be initiated in healthcare facilities as soon as the newborns are clinically stable.[1] Furthermore, SSC is a key part of the UNICEF UK Baby Friendly Initiative standards.[2] SSC can also regulate stress, anxiety and psychological distress of both the mother and the infant.[3]

With the improvement of medicine and neonatology, more and more extreme premature infants survive and are looked after in neonatal units worldwide. Despite this improvement in survival rates, the incidence of BPD remains unchanged over the last two decades.[4]

It has previously been demonstrated that SSC improves physiological outcomes and there are long-term benefits associated with SSC, including reduction in morbidity and mortality.[5,6] However, the effect of SSC on respiratory parameters in infants with bronchopulmonary dysplasia (BPD) and on non-invasive ventilation remains unclear. BPD infants have a prolonged length of stay and can be offered cumulatively many hours of SSC during their admission.

Neurally adjusted ventilatory assist (NAVA) is a mode of respiratory support that uses the electrical activity of the diaphragm (Edi) as a neural trigger to synchronise breaths with the patient's neural respiratory drive. During NAVA, a modified nasogastric feeding tube with electrodes (Edi catheter) monitors the Edi. The Edi waveform determines the delivered pressure from the ventilator.[7,8] On NAVA, the ventilator delivers a pressure that is synchronised and in proportion to the infant's diaphragmatic electrical activity.[9] Synchrony can be achieved even in the presence of significant air leaks, which allows NAVA to be given both invasively via an endotracheal tube (invasive NAVA) and non-invasively (NIV-NAVA) via nasal masks or prongs.[10] NIV-NAVA has been successfully used clinically in neonates as a mode of respiratory support to prevent intubation and allow early extubation.[11] A recently published study assessed NIV-NAVA in infants with evolving or established BPD. This demonstrated that a combination of NAVA/NIV-NAVA compared with conventional invasive and NIV modes may be advantageous in infants born very prematurely and with evolving or established BPD.[12]

The Edi signal can be used to study the breathing effort. The Edi values reflect the patient's work of breathing. Since SSC reduces stress, comforts infants and stabilises their physiological parameters,[3] we hypothesised that respiratory parameters including diaphragmatic electrical activity would improve during SSC. The aim of this study was to determine whether SSC improved respiratory parameters in premature infants with evolving or established BPD receiving NIV-NAVA ventilation.

Key notes

- This study focused on the effect of skin-to-skin (SSC) on respiratory parameters in extremely premature infants when supported on non-invasive NAVA, a novel mode of ventilation used in neonatology.
- We demonstrated an improvement in respiratory parameters in infants receiving SSC with evolving or established BPD.
- Longer term outcomes should be studied to see if the improvement in respiratory parameters leads to a reduction of BPD in the long term.

2 | MATERIAL AND METHODS

We compared respiratory parameters before and at the end of SSC in premature infants with BPD when supported on NIV-NAVA. A prospective cohort study was undertaken between May 2021 and January 2022 on the neonatal unit at St Georges Hospital, London. Premature infants born at less than 32 weeks of gestational age (GA) who were supported with NIV-NAVA were included in this study. Premature infants born at less than 32 weeks of GA requiring invasive ventilation support beyond the second week (14 days) of postnatal age were identified as infants with evolving BPD, and premature infants born less than 32 weeks of GA requiring respiratory support at 36 weeks of corrected gestational age (CGA) were deemed as infants with established BPD.[13] This project was registered with St George's University Hospitals NHS Foundation Trust (SGH) Clinical Effectiveness and Audit department.

NIV-NAVA was delivered by the SERVO-n Maquet Getinge ventilator. A 6-French, 49 or 50 cm long Edi catheter was inserted via orogastric route and correct positioning was confirmed as per instructions of the manufacturer using the Edi catheter positioning guide function on the ventilator (Maquet SERVO-n User Manual Version 4.1). The guide function displays the retrocardiac electrocardiogram (ECG) and correct positioning was confirmed when the P waves and QRS complexes were visible in the uppermost leads and then decreased in size until the P waves disappeared in the lowest lead. Coloured highlighting of the central two leads appeared once the catheter was in the correct place. Once correct positioning was confirmed, the catheter was securely attached to the infant's face using an adhesive dressing.

SSC was offered to parents as per standard practice on the neonatal unit. The parent sat leaning back on a reclining chair at the incubator side and infant was transferred to the parent's chest. Extremely premature babies were placed prone against parent's chest. The infant's lines and tubes were secured over the parent's shoulder. During SSC, the infant's head was covered with a hat and the body was covered by a blanket. Recommended duration of cuddle was at least 1 h.

Demographic characteristics were collected from medical records, such as GA at birth, birth weight (BW) and gender. Respiratory parameters studied were peak electrical activity of the diaphragm (peak Edi or Edi peak), mean airway pressure (P mean), respiratory rate (RR), fraction of inspired oxygen (FiO_2) and percentage of time spent on back-up mode (back up peak inspiratory pressure [PIP]

delivered over the set positive end expiratory pressure [PEEP] when no respiratory effort detected).

SSC episodes were documented by the nurse looking after the baby or the parent on a form attached to the baby's folder. Continuous data were downloaded from the ventilator onto a USB stick and respiratory parameters *pre-SSC* (when baby in the incubator) were compared to *end-SSC* (just before end of SSC). Data compared were an average of 5 min' continuous readings obtained from Edi catheter for *pre-SSC* and *end-SSC*.

2.1 | Statistical analysis

Respiratory parameters *pre-SSC* were compared to *end-SSC*, and then assessed for statistical significance using the Wilcoxon signed-rank test using IBM SPPS statistical software, V.28 (IBM Corporation, USA). A p-value <0.05 was considered to be statistically significant.

3 | RESULTS

A total of 65 episodes of SSC were analysed from 12 premature infants with evolving or established BPD. Median birth GA was 24.4 (23.1–27.0) weeks with a median BW of 642 (530–960) grams. 8/12 (67%) were male and 4/12 (33%) were female. Median corrected GA (CGA) when SSC measurements were performed was 37.4 (29.0–64.9) weeks and median postnatal age was 92 (24–281) days. Total median duration of SSC was 89 (20–250) min. Only 2/12 (17%) infants were on oral sedation; one patient on oral morphine from day 7 postnatal age and one patient on oral clonidine and morphine started on days 8 and 11 postnatally respectively.

Peak Edi, P mean and RR improved at the end of the SSC. Peak Edi was significantly lower in *end-SSC* compared to *pre-SSC* ($p < 0.001$) (Figure 1). Similarly, P mean and RR at the end of SSC were significantly lower when compared to *pre-SSC* ($p = 0.008$ and $p = 0.031$ respectively). There was no statistically significant difference in percentage of inspired oxygen requirement or in the percentage of time spent on back-up mode in *end-SSC* compared to *pre-SSC* ($p = 0.556$ and $p = 0.853$) (Table 1).

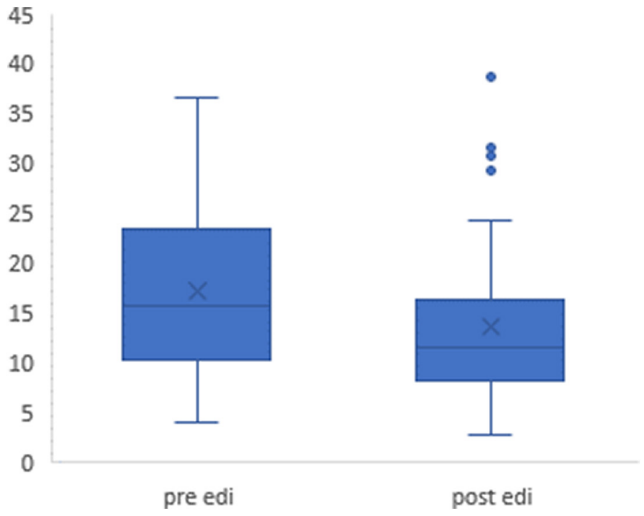

FIGURE 1 Electrical activity of diaphragm (Edi), *pre-SSC* versus *end-SSC* (Box plot).

4 | DISCUSSION

Our study evaluated the effect of SSC on the respiratory parameters in extremely premature infants with evolving or established BPD on NIV-NAVA. We have demonstrated that SSC improved respiratory parameters in this group of patients. The improvement in respiratory parameters was maintained at the end of SSC, which suggests that longer SSC could be more beneficial. There was no statistically significant difference in FiO_2 requirements. This may be explained by a tendency by the care giver to increase FiO_2 just before and during the cuddle.

Recent studies have been published on the effects of SSC on the respiratory physiology of preterm babies.[14–16] Our study showed a significant reduction in diaphragmatic electrical activity. Soukka et al (2014) study also showed a reduction on the electrical activity of the diaphragm, although not in a statistically significant way. They studied the safety of SSC and its effect on diaphragmatic electrical activity in 17 premature infants when on NIV-NAVA. They concluded that SSC was safe in terms of cardiorespiratory stability and that it is not associated with increased neural activity of the diaphragm.[14] Soukka's sample population had a higher median GA at birth of 28 weeks and higher BW of 900 grams, compared to 24.4 weeks and 642 grams in our study. Soukka studied infants recovering from respiratory distress syndrome and the median age at the time of studied SSC was 20 days, whereas we studied infants with evolving or established BPD at an older median age of 92 days. Our aim was not to assess the safety of SSC, but to determine if SSC improved respiratory parameters. Therefore, we studied other respiratory parameters such as P mean, RR, FiO_2 and time spent on back-up mode. To monitor CO_2 levels in blood gas measurements before and at the end of SSC could be an interesting way to interrogate the improvement shown in respiratory parameters, in that an improvement would support the fact that babies were better at the end of SSC and allay any concerns about babies tiring during SSC. However, this would have entailed two additional skin punctures for babies who were very stable and would only routinely undergo blood gas measurement daily or every other day as part of standard unit practice, which we considered too invasive.

We evaluated the effect of SSC on the electrical activity of the diaphragm and we demonstrated its significant improvement in preterm babies when supported on non-invasive NAVA. Kato et al. (2021) also evaluated the effect of SSC on electrical activity of the diaphragm, however, all the infants in their study were intubated and ventilated on invasive NAVA. They concluded that respiratory efforts (as evaluated by Edi) are significantly reduced during SSC in

TABLE 1 Respiratory parameters, *pre-SSC* versus *end-SSC*.

	pre-SSC	*end-SSC*	*p*-Value
Peak Edi (uV)	15.8 (4.0–36.6)	11.5 (2.7–38.7)	<0.001
P mean (cmH_20)	10.3 (7.5–15.5)	9.7 (7.3–15.4)	0.008
RR (breaths/min)	53.4 (35.1–74.1)	52.9 (31.1–78.1)	0.031
FiO_2 (%)	39.0 (26.0–56.1)	40.0 (22.1–56.1)	0.556
Back-up (%/min)	5.1 (0.0–29.3)	5.9 (0.0–56.0)	0.853

Note: Data displayed as median (range).

ventilated preterm infants.[15] Unlike our study, Kato did not investigate the effects on respiratory support measurements such as P mean and FiO_2. Although in both studies baseline study population characteristics were comparable, with a similar GA at birth and BW, the median age when SSC was analysed was significantly different between studies. In our study, SSC was studied at a later postnatal age when chronic lung disease was evolving or established and the baby was on NIV-NAVA (median age 92 days and CGA of 37.4 weeks), compared to babies still ventilated at 41 days and 31.3 weeks in Kato's work.

We demonstrated an improvement of respiratory parameters in a very premature group of patients. Lee et al. (2021) investigated whether SSC stabilised and significantly improved respiratory physiology in preterm infants.[16] Their study showed that respiratory parameters were significantly improved during both invasive NAVA and NIV-NAVA in a less preterm population (when SSC was performed at a CGA ≥28 weeks). However, when performed under 28 weeks of CGA, only the electrical activity of the diaphragm showed an improvement. Therefore, their study sample population was significantly different to ours, with a more mature population and with SSC episodes performed at a younger postnatal age. Their median GA at birth was 27.6 weeks and BW of 1000 grams, compared to 24.4 weeks and 642 grams in our study, and median age at SSC of 29 days with median CGA of 30.7 weeks versus 92 days and CGA of 37.4 weeks in our study. Furthermore, 83% of Lee's episodes were in ventilated infants, whereas in our work, all our infants were supported on NIV-NAVA.

To the best of our knowledge, ours is the only study assessing the effect of SSC in this very significant group of patients: infants born with extreme prematurity and very low birth weight, who undergo SSC at an older postnatal age when BPD is evolving or established and require non-invasive respiratory support. With perinatal care continuously improving, more extremely preterm infants are admitted worldwide. Extremely premature infants are at higher risk of suffering from significant BPD, requiring long admissions and long-term non-invasive ventilation. These long hospital stays could potentially provide more opportunities for SSC.[17–19] Our results demonstrate that these vulnerable patients should receive SSC, despite their challenging respiratory status, as SSC improves their respiratory parameters.

There are strengths and some limitations to this study. Although we had 12 patients in our study, repeated measures of SSC episodes on each patient improved the power of our study and we were able to show a statistically significant effect of SSC on respiratory parameters on NIV-NAVA. This was similar to the limited previous results in younger infants who were more mature at birth, and who were ventilated. Patients were their own controls, and this makes the outcomes more robust, limiting selection bias. All the measured SSC episodes were on infants receiving non-invasive NAVA. Non-invasive ventilation that is not triggered and synchronised proportionally (as in NAVA) may not show the same benefits. Although some of the respiratory parameters did not show a statistically significant improvement, none worsened.

Longer SSC episodes were beneficial as improvements in respiratory parameters were maintained until the end of SCC. Although not analysed in this study, the correlation between duration of SCC episode and reduction on Edi Peak would be very interesting to be analysed in further studies. With longer hospital stays and more opportunities for SSC, we surmise that these patients may be exposed to longer cumulative periods of SSC, which may allow improvements in respiratory parameters over the longer term and which could potentially help protect the developing lung from BPD.

5 | CONCLUSION

In conclusion, SSC improves respiratory parameters in very prematurely born infants with evolving or established BPD on non-invasive NAVA. With increased survival of extremely preterm infants, rates of BPD have largely remained unchanged. Many infants will therefore receive long term, non-invasive respiratory support. SSC has shown short-term benefits in improving respiratory parameters in infants with evolving BPD. Longer term outcomes should be studied to see if this improvement in respiratory parameters translates into a reduction in BPD.

AUTHOR CONTRIBUTIONS

Dr Shetty, Dr Duffy, Dr De-Rooy and Dr Kulkarni designed the study; Dr Serrano-Llop collected the data and submitted the first draft of the manuscript. All authors were involved in the preparation of the manuscript and approved the final manuscript as submitted.

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CONFLICT OF INTEREST

The authors have no financial or other conflicts of interest to declare. No additional funds were required for this study.

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REFERENCES

1. WHO Recommendations on Interventions to Improve Preterm Birth Outcomes. World Health Organization; 2015.
2. UNICEF UK Baby Friendly Initiative. (n.d.). Baby Friendly standards. https://www.unicef.org.uk/babyfriendly/about/standards/
3. Ionio C, Ciuffo G, Landoni M. Parent-infant skin-to-skin contact and stress regulation: a systematic review of the literature. Int J Environ Res Public Health. 2021;18:4695.
4. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ. 2012;345:e7976.
5. Boundy EO, Dastjerdi R, Spiegelman D, et al. Kangaroo mother care and neonatal outcomes: a meta-analysis. Pediatrics. 2016;137:e20152238.
6. Conde-Agudelo A, Díaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database Syst Rev. 2016;8:CD002771.
7. Stein H, Firestone K. Application of neurally adjusted ventilatory assist in neonates. Semin Fetal Neonatal Med. 2014;19:60-69.
8. Beck J, Sinderby C. Neurally adjusted Ventilatory assist in newborns. Clin Perinatol. 2021;48:783-811.
9. Rossor TE, Hunt KA, Shetty S, Greenough A. Neurally adjusted ventilatory assist compared to other forms of triggered ventilation for neonatal respiratory support. Cochrane Database Syst Rev. 2017;10:CD012251.
10. Stein H, Beck J, Dunn M. Non-invasive ventilation with neurally adjusted ventilatory assist in newborns. Semin Fetal Neonatal Med. 2016;21:154-161.
11. Firestone KS, Beck J, Stein H. Neurally adjusted Ventilatory assist for non-invasive support in neonates. Clin Perinatol. 2016;43:707-724.
12. Shetty S, Evans K, Cornuaud P, Kulkarni A, Duffy D, Greenough A. Neurally adjusted ventilatory assist in very prematurely born infants with evolving/established bronchopulmonary dysplasia. AJP Rep. 2021;11:e127-e131.
13. Thébaud B, Goss KN, Laughon M, et al. Bronchopulmonary dysplasia. Nat Rev Dis Primers. 2019;5:78.
14. Soukka H, Grönroos L, Leppäsalo J, Lehtonen L. The effects of skin-to-skin care on the diaphragmatic electrical activity in preterm infants. Early Hum Dev. 2014;90:531-534.
15. Kato Y, Takemoto A, Oumi C, et al. Effects of skin-to-skin care on electrical activity of the diaphragm in preterm infants during neurally adjusted ventilatory assist. Early Hum Dev. 2021;157:105379.
16. Lee J, Parikka V, Lehtonen L, Soukka H. Parent-infant skin-to-skin contact reduces the electrical activity of the diaphragm and stabilizes respiratory function in preterm infants. Pediatr Res. 2022;91:1163-1167.
17. Avila-Alvarez A, Zozaya C, Pértega-Diaz S, et al. Spanish neonatal network SEN1500. Temporal trends in respiratory care and bronchopulmonary dysplasia in very preterm infants over a 10-year period in Spain. Arch Dis Child Fetal Neonatal Ed. 2022;107:143-149.
18. Sand L, Szatkowski L, Kwok TC, et al. Observational cohort study of changing trends in non-invasive ventilation in very preterm infants and associations with clinical outcomes. Arch Dis Child Fetal Neonatal Ed. 2022;107:150-155.
19. Manley BJ, Hodgson KA. Non-invasive ventilation and bronchopulmonary dysplasia: is LESS really MORE? Arch Dis Child Fetal Neonatal Ed. 2022;107:118-119.

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